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INSIGHTS INTO PHYTO PHARMACEUTICAL STUDIES OF BLIND-YOUR-EYE-MANGROVE *EXCOECARIA AGALLOCHA*: A REVIEW

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ABSTRACT
A large variety of plants with varied medicinal and pharmacological implications are used in the traditional system of medicine. Excoecaria agallocha L. (Euphorbiaceae), a significant mangrove plant, is reviewed in detail in this article, along with its ethnobotany, Phytochemistry, and pharmacological effects. It has historically been used to cure a number of illnesses, including epilepsy, ulcers, leprosy, rheumatism, and paralysis. It is also known as the blind-your-eye mangrove plant because the latex extracted from the bark has a poisonous nature and has the potential to temporarily blind people. Many phytoconstituents, primarily diterpenoids, triterpenoids, flavonoids, sterols, and a few other compounds, have been isolated from the plant. The leaves, stem, latex, and root extracts incorporated 20 distinct polyphenols, 15 terpenoids, and more than 50 volatile components. The plant also shows a wide range of pharmacological properties, including antioxidant, antibacterial, anti-inflammatory, analgesic, antiulcer, anticancer, antireverse transcriptase, antihistamine-release, antifilarial, DNA damage protective, antidiabetic, and antitumor protecting properties. Therefore, this study might assist researchers who seek to conduct additional research in these domains.

KEYWORDS: Mangroves; Thillai; Terpenoids; Rutin; Antidiabetic; Diterpenoids; Euphorbiaceae; Excoecaria agallocha; Mangrove; Pharmacology; Phytoconstituents.

BACKGROUND
Mangroves are a group of plants that grow in tropical and subtropical coastal intertidal zones. A vast majority of the trees and shrubs in the mangrove community have broad, leathery, all-year-long leaves and are salt-tolerant. Some tree roots develop downward from the main stem and branches, acting as stilts in an unstable, slippery base. An ancient mangrove species known as "Tala virucham" in Tamil may be found at the Chidambaram shrine of "Tillai Lord Nataraja," called Excoecaria agallocha L. (Euphorbiaceae). Excoecaria agallocha's common names include "Agallocha," "blinding tree," "Tillai," "Kampetti," "Tilla," "Tella," and "Chilla" in Telugu, as well as "Thelakiriya," "Thalia," in Singhalese. It can be found in abundance in Pichavaram Mangrove Forest, Indian Coastal Regions, and Australia, from Northern New South Wales around to Western Australia. It is a least-concern position in accordance with Red List criteria[1] (Systematic classification) (Figure 1). The majority of people around the world rely entirely or partially on the traditional medical system to meet their essential medical needs. According to a 1993 World Health Organisation survey, traditional physicians in India, Bangladesh, and Burma handle about 80%, 90%, and 85% of patients, respectively.[2] In recent years, developed as well as developing nations have used more health remedies made from plants, which has caused the market for herbal products to raise rapidly worldwide. The study of herbals has revealed an increased trend.[3]

1. INTRODUCTION
Mangroves are a group of plants that live in tropical and subtropical coastal intertidal zones. The vast majority of the trees and shrubs in the mangrove community feature broad, leathery, all year round leaves and are salt tolerant. Some tree roots extend vertically downward from its primary stem and branches, functioning as stilts in an unstable, sloppy base. Many additional roots radiate out into the air like sticks, knobs, or loops or they simply snake around the tree in a serpentine pattern, being completely exposed during low tide. These roots are designed to draw in air for breathing because the oxygen-poor water-logged soil is lacking. Mangroves are resilient. Mangroves reside in warm, dirty, and salted instances which might prove fatal other vegetation swiftly mainly since their roots are submerged in water. What is their method? The mangrove maintains itself standing up during the transition soil during which both earth and sea converge via an assortment of incredible modifications, such as a sophisticated base network plus

a filtering mechanism which blocks away most every bit of salinity. Not only do mangroves persist in harsh environments, but its ecosystem also supports a staggering variety of animals, some of those only exist in mangrove forests.[4]

1.1 Plant introduction

Excoecaria is a genus comprised of approximately forty species prevalent in the mangrove habitats of Asia, Africa, and northwest Australia.[5] The milky latex exuded by *Excoecaria agallocha* bark is potentially hazardous and can lead to brief visual impairment and epidermal scorching.[6] The latex is also renowned for its biocidal properties that harm aquatic creatures and phytoplankton, as well as for creating metabolic downturn in the rice field crab, Oziotelphusa senex, and for consumption as an uterotonic, fish poison, dart poison, and for harbouring intriguing chalcones and Piperidine alkaloids.[7] *E. agallocha* leaves primarily shed once a year. Unlike greater mangrove species, they lack distinctive aerial roots referred to pneumatophores, which extend above the soil surface providing oxygen to the below the surface roots.[8]

Fig. 1: *Excoecaria agallocha*. Linn.

1.2 Vernacular names[9]

Telugu: Thilla
Hindi: Gangiva, Tejbala
English: Milky mangrove, blind-your-eye-mangrove
Sanskrit: Agaru, Gangwa, Gaourai
Bengali: Gewa
Malayalam: Komatti, Kammetti, Kannampotti

1.3 Botanical description

Botanical name: *Excoecaria agallocha*. Linn

Synonyms[9, 10]

Excoecaria affinis Endl.
Excoecaria camettia Willd.
Stillingia agallocha L.
Commia cochinchinensis, Lour.
Excoecaria agallocha var. lancifolia, Pax & K. Hoffm.
*Excoecaria agallocha var. orthostichalis*Mull. Arg
Excoecaria agallocha var.dallachyana, Baill.
Excoecaria agallocha var. muelleriana, Baill.
Excoecaria agallocha var.ovalis (Endl.), Mull. Arg.

Common name[9]

Blind-Your-Eyes,
Buta-Buta, Bebuta,
Milky Mangrove,
Kayu Buta-buta,
Kampetti,
Thilla, Tilai.

Taxonomical classification[9]

Kingdom: Plantae
Phylum: Charophyta
Class: Equisetopsida
Subclass: Magnoliidae
Order: Malpighiales
Family: Euphorbiaceae
Genus: *Excoecaria*
Species: *E. agallocha* Linn.

Biogeographical distribution[11]

Native distribution: From India and Sri Lanka, to Taiwan, southern Japan, Southeast Asia, Papua New Guinea, Northern Australia, and the Pacific Islands.
Native habitat: Shoreline (Mangrove Forest)
Preferred climate zone: Tropical, Sub-Tropical, and Monsoonal climate zones are preferred.

Morphology[9,11]

It is a 15 m tall, heavily branched tree. Its bark is warty, grayish-brown, and has lenticels and vertical fissures. Any broken portion of the plant discharges a white latex material. It also loses its leaves immediately before the start of flowering since it is deciduous.
Stem: Bark exudate rapid and copious, sometimes deciduous.
Roots: Roots run along the ground surface and often knotted and covered with lenticels.
Leaves: Leaves alternate, thick, oval and pointed (5-10cm long), arranged alternately in a spiral. Young leaves are pink, old leaves turn yellow then red before dropping off. Leaves usually drop off after dry weather.
Flowers: Flowers are tiny (less than 1mm). Trees bear either male or female flowers, never both. Male flowers start as upright narrow cones when young and as they develop, elongate into longer spikes (5-10cm) that

eventually form drooping yellow tassels. Male flowers are said to be "very scented". Female flowers appear in shorter spikes.

Fruits & Seeds: Fruits 3-lobed, about 8 mm diameter. Seeds are about 4mm long. Radicle is about 1 mm long.

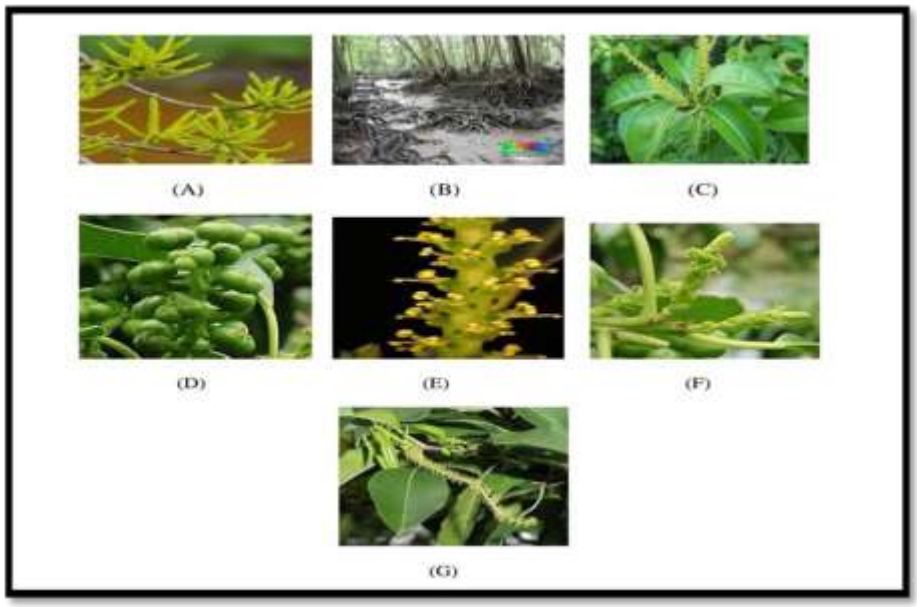


Fig. 2: Parts of *Excoecaria agallocha* Linn. (A) Flowering branches (B) Roots (C) Leaves (D) Fruits (E) Flowers (F) Female flowers (G) Male flowers.

2. Uses

2.1 Ayurvedic uses[12]

Studying the effects of E. agallocha extracts pharmacologically revealed

1. Antioxidant and antibacterial
2. Antiviral
3. Anticancer
4. Anti-inflammatory and analgesic
5. Treatment of Epilepsy
6. Reduce Ulcers
7. Leprosy
8. Rheumatism and paralysis

2.2 Traditional medicinal uses[9]

1. Additionally, it has been traditionally used to treat dermatitis, haematuria, and conjunctivitis.
2. This plant secretes latex, which has been used as a purgative, abortifacient, and to cure rheumatism, paralysis, ulcers, and leprosy.
3. The indigenous populations of Malaysia, India, and New Caledonia use the leaves and latex of this plant as fish poison.
4. The wood and bark are used to alleviate flatulence in Thailand.
5. Leprosy is alleviated in Sri Lanka with the smoke from wood being burned, and swellings of the hands and feet are dealt with the root pounded with ginger.
6. The oil extracted from the woods is used by the Malays to treat skin infections and irritation.
7. The plant's roots are used to alleviate swellings and toothaches.

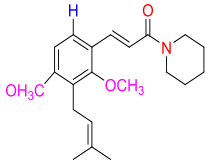
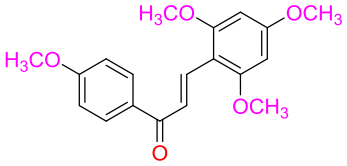
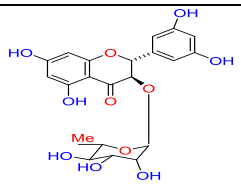
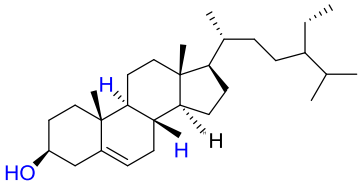
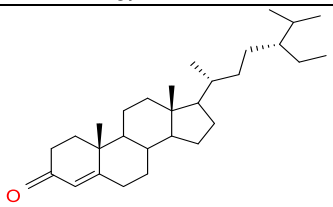
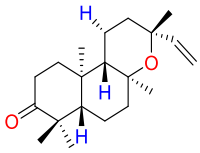
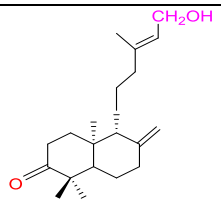
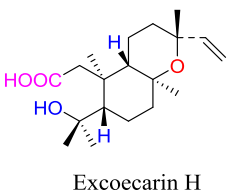
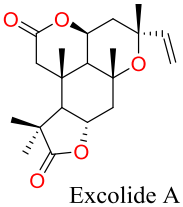
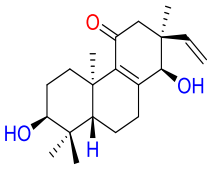
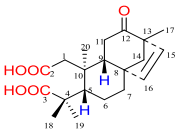
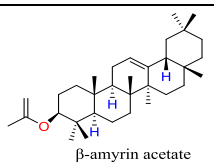
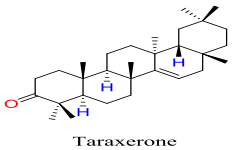
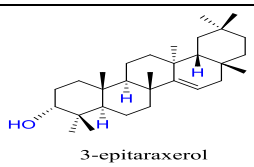
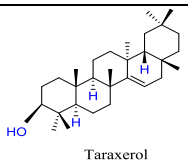
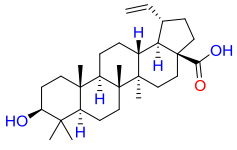
3. Phytochemical properties[14-20]

Table 1: Phytochemical review of *Excoecaria agallocha* Linn.

S. NO.	Plant part with extract	Isolated compounds	Title of the work	Author	Journal (year)
1.	Petrol extract of Stem wood	Piperidine - alkaloid	A Piperidine Alkaloid from *Excoecaria agallocha*.	Satya Prakash, et.al	Phytochemistry (Elsevier), Pergamon (1982)
2.	Ethyl acetate & Acetone extracts of Latex	3,5 – tetracadienoate & 3,5,7 – hexadecatrienoate (Daphnane & Tigliane types)	Cryptic & free skin irritants of Daphnane & Tigliane types in latex of *Excoecaria agallocha*.	C. Karalai, et.al	Planta Med (1993)
3.	Dichloromethane	Phorbol ester	Novel Phorbol ester	Karen L.	Journal of Natural

	& Methanolic extracts of leaves and bark twigs		from *Excoecaria agallocha*.	Erickson, et.al	Products (1995)
4.	Ether extract of Wood	Excoecarins A, B & C	Chemical structures of Excoecarins A, B & C: three new Labdane type diterpenes from wood, *Excoecaria agallocha*.	Tenji Konishi, et.al	Chem. Pharm. Bull (1996)
5.	Ether extract of Resinous Wood	Excoecarin H	Stereostructure of Excoecarin H, a novel seco-Labdane-type diterpene from *Excoecaria agallocha*.	Tenji Konishi, et.al	Chem. Pharm. Bull (1997)
6.	Ether extract of Resinous Wood	Labdane-type Diterpenes	Five new Labdane diterpenes from *Excoecaria agallocha*.	Tenji Konishi, et.al	Chem. Pharm. Bull (1998)
7.	Ether extract of Wood	Excoecarins F, G1, G2 & Labdane type diterpenoids	Stereostructures of new Labdane-type diterpenes, Excoecarins F, G1, G2 from wood of *Excoecaria agallocha*	Tenji Konishi, et.al	Chem. Pharm. Bull (1999)
8.	Hexane extract of Roots	Agallochins A-E diterpenoids	Five diterpenoids (Agallochins A-E) from mangrove plant *Excoecaria agallocha* Linn.	A.S Anjaneyulu, V L Rao.	Elsevier.com/ locate / phytochem, 55 Pergamon. (2000)
9.	Ethyl acetate extract of resinous wood	Diterpenes and Excoecarins M & N	Novel diterpenes, excoecarins M and N from resinous wood of *Excoecaria agallocha* Linn.	Tenji Konishi et al.	Tetrahedron letters 41, Pergamon. (2000)
10.	Acetone extract of Stem	Excoecarins V1-V3 diterpenoids & Flavone glycoside	Three diterpenoids (Excoecarins V1-V3) & a flavone glucoside from fresh stem of *Excoecaria agallocha*.	Tenji Konishi, et.al	Chem. Pharm. Bull (2003)

➢ **Chemical structures of *excoecaria agallocha* Linn.**

Compounds	Structures
Alkaloids	 2,4-dimethoxy-3-ψ,ψ-dimethylallyl -trans-cinnamoylpiperidide
Flavonoids	 2′,4′,6′,4-tetramethoxychalcone  3,5,7,3',5'-pentahydroxy-2R,3R-flavanonol 3-O-α-L-rhamnopyranoside
Sterols	 β-sitosterol  β-sitostenone
Diterpenes	 ent-3-oxo-13-epi-manoyl oxide(Ribenone)  ent-15-hydroxylabda-8(17),13E-dien-3-one  Excoecarin H  Excolide A   Agallochaol A ent-12-oxo-2,3-secobeyer-15-ene-2,3-dioicacid
Triterpenoids	 β-amyrin acetate  Taraxerone  3-epitaraxerol  Taraxerol  Betulinic acid

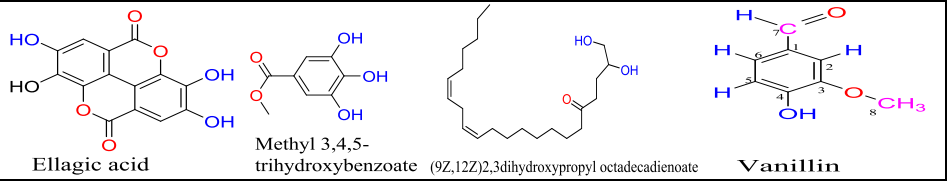
Others	 Ellagic acid; Methyl 3,4,5-trihydroxybenzoate; (9Z,12Z)2,3dihydroxypropyl octadecadienoate; Vanillin

Table 2: [Chemical structures of Alkaloids – 2, 4-dimethoxy-3-ψ, ψ-dimethylallyl-*trans*-cinnamoylpiperidide,[21] Flavonoids - 2′, 4′, 6′,4-tetramethoxychalcone,[21] 3,5,7,3′,5′-pentahydroxy-2 *R* ,3 *R* -flavanonol 3- *O* -α- L – rhamnopyranoside,[22] Sterols – β-sitosterol & β-sitostenone,[23] Diterpenes – *ent*-3-oxo-13-epi-manoyl oxide (Ribenone),[17] *ent*-15-hydroxylabda-8(17), 13*E*-dien-3-one,[24] excoecarin H,[19] Excolide A,[25] Agallochaol A,[26] *ent*-12-oxo-2, 3-secobeyer-15-ene-2, 3-dioic acid,[15] β-amyrin acetate,[27] Taraxerone,[27] 3-epitaraxerol [27], Taraxerol,[27] Betulinic acid,[28] Ellagic acid,[29] Methyl 3,4,5- trihydroxybenzoate,[15] (9Z, 12Z) 2,3 dihydroxypropyl octadecadienoate,[28] Vanillin].

4. Pharmacological properties

4.1 Antitumor protecting activity[30]

From potent resinous woods of E. agallocha, seven diterpenoids have been recognised. These compounds showed a noteworthy ability to prevent the activation of the Epstein-Barr virus (EBV), which had been triggered by the tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA). Apart from that, in a two-stage carcinogenesis assay of mice tumours implementing 7, 12-dimethylbenz[a] anthracene (DMBA) as an initiator and TPA as a promoter, ent-3 β-hydroxy-15-beyeren-2-one (82) shown outstanding antitumor promoting activity in vivo.

4.2 Antidiabetic activity[31]

Thirumurugan et al. examined the antidiabetic activity of E. agallocha leaves in alloxan-induced diabetic mice. The results demonstrated that the ethanolic leaves extract has substantial advantages hypoglycemic effect in both the normal and alloxan-induced diabetic mice at a dose of 500 mg/kg.

4.3 DNA damage protective activity[5]

Poorna et al. (2012) reported on the DNA damage-preventive properties of E. agallocha leaves, especially the water portions of the leaf extract demonstrating notable effectiveness in preventing DNA damage.

4.4 Antifilarial activity[32]

Significant antifilarial action in a dose-dependent response was experimentally shown by the methanolic leaf extract of E. agallocha, as evidenced by the mortality of the metazoan filarial parasite Setaria digitate at different stages of development. Following a 24-hour exposure to methanolic leaf extracts at concentrations of 10, 50, and 100 µg /ml, almost thirty percent, 75%, and 90% of S. digitata's embryonic stages were determined to be dead, respectively.

4.5 Antihistamine-release activity[33]

Hossain et al. explored the antihistamine-release activity of E. agallocha bark on an ionophore A23187-induced histamine-release assay model. The findings showed that ethanol and distilled water endured more substantial antihistamine-release activity than other fractions comparable to hexane, chloroform, and ethyl acetate.

4.6 Antireverse transcriptase activity[34, 35]

Patil et al. (2011) showed the ethanol extract of E. agallocha stems exhibited antireverse transcriptase action. The outcomes of the investigation demonstrated that the stem ethanol extract's activity-guided ethanol fraction displays strong antireverse transcriptase efficacy.[34] By reducing the concentrations of p24 and reverse transcriptase in the supernatant, an efficacious in vitro inhibitor of HIV-1 replication was identified—a new Phorbol ester with an IC50 of 6 nm.[35]

4.7 Anticancer activity[34]

The activity-guided fraction of the ethanol extract of E. agallocha stem was exploited by Patil et al. (2011) to report anticancer activity using the MTS in vitro assay. The results demonstrated high activity against the pancreatic cancer cell lines Capan-1 and Miapaca-2, with IC50 values of 4 µg /ml and 7 µg /ml, respectively.

4.8 Antiulcer activity[37]

The antiulcer activity of E. agallocha leaves was investigated in rats with ulcers resulting from non steroidal anti-inflammatory drugs. The findings indicated that the leaf extract may both reduce acidity and strengthen the mucosal defence in the stomach region. As consequence, the plant's leaves have antiulcerogenic characteristics.

4.9 Anti-inflammatory activity[38]

In a carrageenan-induced rat paw edoema model, Babuselvam et al. considered the acute inflammatory properties of ethanol in water (3:1) extract of many different components of E. agallocha, consisting of latex, leaves, and seeds. The outcomes showed statistically significant activity at an intake of 500 mg/kg, in contrast to the control, causing an inhibition of 63.15%, 62.15%, and 69.69% in latex, leaves, and seeds, respectively. Contrary to expectations, the seed extract displayed maximum activity at a dose of 500 mg/kg in the cotton pellet-induced granuloma test, which was 57.03% greater than the control.

4.10 Analgesic activity[38]

Babuselvam et al. researched the analgesic effect of ethanol: water (3:1) extract of E. agallocha leaves, seeds, and latex; of these, extract from seeds drastically lowered the number of writhes in 20 min and also increased the percentage of inhibition in the test organisms' acetic acid writhing test. Apart from that, in the tail immersion model, the 500 mg/kg concentration of the seed extract reveals its greatest activity (80.29%) in comparison to the control.

5. CONCLUSION

There have been instances in traditional medicine that various parts of E. agallocha L., such as the leaves, roots, woods, stems, bark, latex, and seeds, have therapeutic potential for the treatment of various ailments. These include antitumor-preventive, antidiabetic, antimicrobial, anti-inflammatory, analgesic, antiulcer, anticancer, antireverse transcriptase, antifilarial, and protective contrary to DNA damage. Distinct plant sections yielded a number of chemically active substances that belonged to many different chemistry classifications. Diterpenoids of the labdane, isopimarane, kaurane, Beyerane, artisane, Daphnane, and Tigliane types were the majority of those that were isolated. Triterpenoids, flavonoids, alkaloids, sterols, tannins, and a few other unidentified chemicals (such as organic acids, organic acid esters, and alcohol derivatives) make up the majority of the other phytoconstituents that have been isolated. This study emphasises a number of pharmacological and phytochemical investigations that have shown E. agallocha L.'s medicinal benefits and phytochemical particulates.

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